

Dkt. 70442-PCT-US/JPW/BJA

THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Eric Kandel, et al.

U.S. Serial No. : 10/582,303

Filed : as §371 national stage of

PCT/US2004/041388, filed December 9, 2004

For : GRP RECEPTOR-RELATED METHODS FOR TREATING

AND PREVENTING FEAR-RELATED DISORDERS

1185 Avenue of the Americas New York, New York 10036 July 18, 2007

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following items numbered 1-61 which are also listed on the accompanying substitute Form PTO-1449, attached hereto as **Exhibit A**. Items 1-9 are either U.S. patents or U.S. patent application publications. Pursuant to 37 C.F.R. 1.98(a)(2)(ii), no copies of references 1-9 are being included herewith. Copies of items 10-61 are attached hereto as **Exhibits 1-52**, respectively. Applicants request that the Examiner review the items listed and make them of record in the subject application.

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(b)(3), before the issuance of a first Office Action on the merits. Accordingly, no fee is required.

- 1. U.S. Patent No. 4,870,009, issued to Evans et al. on September 26, 1989;
- U.S. Patent No. 6,552,061, issued to Kitazawa et al. on April 22, 2003;

A Phy

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 2

- U.S. Patent No. 5,741,651 issued to Feldman et al. on April 21, 1998;
- 4. U.S. Patent No. 5,814,463, issued to Spindel et al. on September 29, 1998;
- U.S. Patent No. 6,817,756, issued to Lee et al. on February 13, 2001;
- 6. U.S. Patent No. 6,200,546, issued to Hoffman et al. on March 13, 2001;
- 7. U.S. Patent No. 5,620,955, issued to Knight et al. on April 15, 1997;
- 8. U.S. Patent No. 6,307,017, issued to Coy et al. on October 23, 2001:
- 9. U.S. Patent No. 6,566,080, issued to Kopin et al. on May 20, 2003;
- 10. Bachevalier, J. et al. (2001). Effects of selective neonatal temporal lobe lesions on socioemotional behavior in infant rhesus monkeys (Macaca mulatta). Behav. Neurosci. 115(3), 545-559 (Exhibit 1);
- 11. Baron-Cohen, S. et al. (2000). The amygdala theory of autism. Neurosci. Biobehav. Rev. 24(3), 355-364 (Exhibit 2);
- 12. Bast, T. et al. (2001). The ventral hippocampus and fear conditioning in rats. Different anterograde amnesias of fear

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 3

after tetrodotoxin inactivation and infusion of the GABA(A) agonist muscimol. Exp. Brain Res. 139(1), 39-52 (Exhibit 3);

- 13. Belmont, L.D., and Mitchison, T.J. (1996). Identification of a protein that interacts with tubulin dimers and increases the catastrophe rate of microtubules. Cell 84(4), 623-631 (Exhibit 4);
- 14. Bolshakov, V.Y. et al. (1997). Recruitment of new sites of synaptic transmission during the cAMP-dependent late phase of LTP at CA3-CA1 synapses in the hippocampus. Neuron 19(3), 635-651 (Exhibit 5);
- 15. Bolshakov, V.Y. et al. (2000). Dual MAP kinase pathways mediate opposing forms of long-term plasticity at CA3-CA1 synapses. Nat. Neurosci. 3(11),1107-1112 (Exhibit 6);
- 16. Bourtchouladze, R. et al. (1998). Different training procedures recruit either one or two critical periods for contextual memory consolidation, each of which requires protein synthesis and PKA. Learn. Mem. 5(4), 365-374 (Exhibit 7);
- 17. Brauer, A.U. et al. (2001). Perforant path lesion induces upregulation of stathmin messenger RNA, but not SCG10 messenger RNA, in the adult rat hippocampus. Neuroscience 102(3), 515-526 (Exhibit 8);
- 18. Cook, E.H. et al. (1998). Linkage-disequilibrium mapping of autistic disorder, with 15q11-13 markers. Am. J. Hum. Genet. 62(5),1077-1083 (Exhibit 9);
- 19. Davis, M., and Whalen, PJ. (2001). The amygdala: vigilance and

Applicants: Eric Kandel, et al.

U.S. Serial No.: 10/582,303

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 4

emotion. Mol. Psychiatry 6(1), 13-34 (Exhibit 10);

- 20. Dulac, C., and Axel, R. (1995). A novel family of genes encoding putative pheromone receptors in mammals. Cell 83(2), 195-206 (Exhibit 11);
- 21. Fanselow, M.S., and LeDoux, J.E. (1999). Why we think plasticity underlying Pavlovian fear conditioning occurs in the basolateral amygdala. Neuron 23(2), 229-232 (Exhibit 12);
- 22. Frederickson, C.J. et al. (2000). Importance of zinc in the central nervous system: the zinc-containing neuron. J. Nutr. 130, 1471S-1483S (Exhibit 13);
- 23. Goddard, A.W. et al. (2001). Reductions in occipital cortex GABA levels in panic disorder detected with ¹H-magnetic resonance spectroscopy. Arch. Gen. Psychiatry 58(6), 556-561 (Exhibit 14);
- 24. Hampton, L.L. et al. (1998). Loss of bombesin-induced feeding suppression in gastrin-releasing peptide receptor-deficient mice.

 Proc. Natl. Acad. Sci. USA 95, 3188-3192 (Exhibit 15);
- 25. Harrel, A.V. et al. (2001). Transgenic mice over-expressing the 5-HT3 receptor have enhanced learning in latent inhibition and contextual fear conditioning paradigms. Soc. Neurosci. Abstr., Program No. 853.11, 31st Annual Meeting, San Diego, California (Exhibit 16);
- 26. Hellmich, M.R. (1999). Multiple protein kinase pathways are involved in gastrin-releasing peptide receptor-regulated secretion. J. Biol. Chem. 274(34), 23901-23909 (Exhibit 17);

Applicants: Eric Kandel, et al.
U.S. Serial No.: 10/582,303
Filed: as §371 national stage of PCT International
Application No. PCT/US2004/041388, filed December 9, 2004
Page 5

- 27. Huang, Y.Y., and Kandel, E.R. (1998). Postsynaptic induction and PKA-dependent expression of LTP in the lateral amygdala. Neuron 21(1), 169-178 (Exhibit 18);
- 28. Hubank, M., and Schatz, D.G. (1994). Identifying differences in mRNA expression by representational difference analysis of cDNA. Nucleic Acids Res. 22(25), 5640-5648 (Exhibit 19);
- 29. Ishikawa-Brush, Y. et al. (1997). Autism and multiple exostoses associated with an X;8 translocation occurring within the *GRPR* gene and 3' to the *SDC2* gene. Hum. Mol. Genet. 6(8), 1241-1250 (Exhibit 20);
- 30. Johansson, B. et al. (2001). Hyperalgesia, anxiety, and decreased hypoxic neuroprotection in mice lacking the adenosine Al receptor. Proc. Natl. Acad. Sci. USA 98(16), 9407-9412 (Exhibit 21);
- 31. Kapp, B.S. et al. (1992). Amygdaloid contributions to conditioned arousal and sensory information processing. In: The Amygdala: Neurobiological Aspects of Emotion, Memory, and Mental Dysfunction, J.P. Aggleton, ed. (New York: Wiley-Liss), pp. 229-254 (Exhibit 22);
- 32. Krezel, W. et al. (2001). Increased anxiety and synaptic plasticity in estrogen receptor β-deficient mice. Proc. Natl. Acad. Sci. USA 98(21), 12278-12282 (Exhibit 23);
- 33. Kroog, G.S. et al. (1995). Mammalian bombesin receptors. Med. Res. Rev. 15, 389-417 (Exhibit 24);
- 34. LeDoux, J.E. (2000). Emotion circuits in the brain. Annu. Rev.

Applicants: Eric Kandel, et al. U.S. Serial No.: 10/582,303 Filed: as §371 national stage of PCT International Application No. PCT/US2004/041388, filed December 9, 2004 Page 6

Neurosci. 23, 155-184 (Exhibit 25);

- 35. Lee, K. et al. (1999). Bombesin-like peptides depolarize rat hippocampal interneurones through interaction with subtype 2 bombesin receptors. J. Physiol. 518(3), 791-802 (Exhibit 26);
- 36. Low, K. et al. (2000). Molecular and neuronal substrate for the selective attenuation of anxiety. Science 290,131-134 (Exhibit 27);
- 37. Mahanty, N.K., and Sah, P. (1998). Calcium-permeable AMPA receptors mediate long-term potentiation in interneurons in the amygdala. Nature 394, 683-687 (Exhibit 28);
- 38. Malleret, G. et al. (1999). 5-HT1B receptor knock-out mice exhibit increased exploratory activity and enhanced spatial memory performance in the Morris water maze. J. Neurosci. 19(14), 6157-6168 (Exhibit 29);
- 39. McKernan, M.G., and Shinnick-Gallagher, P. (1997). Fear conditioning induces a lasting potentiation of synaptic currents in vitro. Nature 390, 607-611 (Exhibit 30);
- 40. McKernan, R.M. et al. (2000). Sedative but not anxiolytic properties of benzodiazepines are mediated by the GABA(A) receptor alpha(1) subtype. Nat. Neurosci. 3(6), 587-592 (Exhibit 31);
- 41. Merali, Z. et al. (1998). Aversive and appetitive events evoke the release of corticotropin-releasing hormone and bombesin-like peptides at the central nucleus of the amygdala. J. Neurosci. 18, 4758-4766 (Exhibit 32);

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 7

- 42. Mermelstein, P.G., et al. (2000). Critical dependence of cAMP response element-binding protein phosphorylation on L-type calcium channels supports a selective response to EPSPs in preference to action potentials. J. Neurosci. 20(1), 266-273 (Exhibit 33);
- al. (2002).43. Parent, M.B. et Effects of the antidepressant/antipanic drug phenelzine and its putative metabolite phenylethylidenehydrazine on extracellular aminobutyric acid levels in the striatum. Biochem. Pharmacol. 63, 57-64 (Exhibit 34);
- 44. Pitkanen, A. et al. (1997). Organization of intra-amygdaloid circuitries in the rat: an emerging framework for understanding functions of the amygdala. Trends Neurosci. 20(11), 517-523 (Exhibit 35);
- 45. Ramboz, S. et al. (1998). Serotonin receptor 1A knockout: an animal model of anxiety-related disorder. Proc. Natl. Acad. Sci. USA 95(24), 14476-14481 (Exhibit 36);
- 46. Rammes, G. et al. (2000). Synaptic plasticity in the basolateral amygdala in transgenic mice expressing dominant-negative cAMP response element-binding protein (CREB) in forebrain. Eur. J. Neurosci. 12, 2534-2546 (Exhibit 37);
- 47. Rogan, M.T. et al. (1997). Fear conditioning induces associative long-term potentiation in the amygdala. Nature 390, 604-607 (Exhibit 38);
- 48. Romanski, L.M., and LeDoux, J.E. (1992). Equipotentiality of

Applicants: Eric Kandel, et al.

U.S. Serial No.: 10/582,303

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 8

thalamo-amygdala and thalamo-cortico-amygdala circuits in auditory fear conditioning. J. Neurosci. 12(11), 4501-4509 (Exhibit 39);

- 49. Schaeren-Wiemers, N., and Gerfin-Moser, A. (1993). A single protocol to detect transcripts of various types and expression levels in neural tissue and cultured cells: in situ hybridization using digoxigenin-labeled cRNA probes. Histochemistry 100, 431-440 (Exhibit 40);
- 50. Sharif, T.R. et al. (1997). Functional expression of bombesin receptor in most adult and pediatric human glioblastoma cell lines; role in mitogenesis and in stimulating the mitogenactivated protein kinase pathway. Mol. Cell. Endocrinol. 130, 119-130 (Exhibit 41);
- 51. Steele, P.M., and Mauk, M.D. (1999). Inhibitory control of LTP and LTD: stability of synapse strength. J. Neurophysiol. 81, 1559-1566 (Exhibit 42);
- 52. Trepel, C., and Racine, R.J. (2000). GABAergic modulation of neocortical long-term potentiation in the freely moving rat. Synapse 35(2), 120-128 (Exhibit 43);
- 53. Tsvetkov, E. et al. (2002). Fear conditioning occludes LTP-induced presynaptic enhancement of synaptic transmission in the cortical pathway to the lateral amygdala. Neuron 34(2), 289-300 (Exhibit 44);
- 54. Wada, E. et al. (1997). Generation and characterization of mice lacking gastrin-releasing peptide receptor. Biochem. Biophys. Res. Commun. 239, 28-33 (Exhibit 45);

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 9

- 55. Wang, C. et al. (2001). Role of NMDA, non-NMDA, and GABA receptors in signal propagation in the amygdala formation. J. Neurophysiol. 86, 1422-1429 (Exhibit 46);
- 56. Weisskopf, M.G., and LeDoux, J.E. (1999). Distinct populations of NMDA receptors at subcortical and cortical inputs to principal cells of the lateral amygdala. J. Neurophysiol. 81, 930-934 (Exhibit 47);
- 57. Weisskopf, M.G. et al. (1999). L-type voltage-gated calcium channels mediate NMDA-independent associative long-term potentiation at thalamic input synapses to the amygdala. J. Neurosci. 19(23), 10512-10519 (Exhibit 48);
- 58. Woodson, W. et al. (2000). Afferents from the auditory thalamus synapse on inhibitory interneurons in the lateral nucleus of the amygdala. Synapse 38(2), 124-137 (Exhibit 49);
- 59. Yu, B., and Shinnick-Gallagher, P. (1997). Dihydropyridine- and neurotoxin-sensitive and -insensitive calcium currents in acutely dissociated neurons of the rat central amygdala. J. Neurophysiol. 77(2), 690-701 (Exhibit 50);
- 60. International Preliminary Report on Patentability (Chapter I) issued by the International Bureau on behalf of the International Searching Authority on June 12, 2006 in connection with International Application No. PCT/US2004/041388 (Exhibit 51); and
- 61. PCT/US2004/041388, filed December 9, 2004, published as WO 05/60625 on July 7, 2005 (Exhibit 52).

Filed: as §371 national stage of PCT International

Application No. PCT/US2004/041388, filed December 9, 2004

Page 10

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Supplementary Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:

Mail Stop Amendment

Commissioner for Patents,

P.O. Box 1450

John P. White Date

Reg. No. 28,678

John P-White

Registration No. 28,678 Attorney for Applicants Cooper & Dunham LLP 1185 Avenue of the Americas New York, NY 10036

(212) 278-0400

Exhibit A

		29
Form PTO	-1449 ⁰ '	4
Substitute	/	~
	JUL!	2 0 2007
	A PART	.6

U.S. Department of Commerce Patent and Trademark Office

rce	whi
:e	Fili

Application Number 10/582,303

Filing Date As §371 national stage of PCT/US04/41388, filed December 9, 2004

First Named Inventor Eric Kandel et al.

Art Unit

Examiner Name

Attorney Docket No. 70442-PCT-US

INFORMATION MAISSENSURE STATEMENT

(Use several sheets if necessary)

U.S. PATENT DOCUMENTS Document Number Number-Kind Code^{2 (if known)} **Publication Date** Examiner Cite Name of Patentee or Applicant of Cited Document Initials No. MM-DD-YYYY U.S. 4,870,009 09-26-1989 Evans et al. U.S. 6,552,061 04-22-2003 Kitazawa et al. U.S. 5,741,651 Feldman et al. 04-21-1998 U.S. 5,814,463 09-29-1998 Spindel et al. U.S. 6,817,756 02-13-2001 Lee et al. U.S. 6,200,546 03-13-2001 Hoffman et al. U.S. 5,620,955 04-15-1997 Knight et al. U.S. 6,307,017 10-23-2003 Coy et al. U.S. 6,566,080 05-20-2003 Kopin et al.

FOREIGN PATENT DOCUMENTS

Examiner Cite No. 1		Foreign Patent Document Country Code ⁵ Number Kind Code ⁵ (If known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	T ⁶
		WO 05/60625	07-07-2005		
_					
EXAMINER SIGNATUR			DATE CONSIDERED		

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). See Kinds of Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. There Office that issued the document, by the two-letter code (WIPO Standard ST.3). For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. Applicant is to place a check mark here if English Language Translation is attached.

Applicants: Eric Kandel, et al. U.S. Serial No.: 10/582.303 Filed: as §371 national stage of PCT/US2004/041388, filed December 9, 2004

Exhibit A

Dame DE	O 144	0 II C Department of Commerce	Application Number	10/582,303	
Form PT		•		·	nul utaga
Substitute		Patent and Trademark Office	Filing Date	As §371 nation of PCT/US04/ filed Decembe	41388,
			First Named Inventor		
INICODA	TA TELO	ON DISCLOSURE CITATION	Art Unit	Isric Kandere	t ai.
i .				_	• • •
(Use severa	il sheets	s if necessary)	Examiner Name	70442 DCT II	
			Attorney Docket No.	70442-PC1-U	<u> </u>
		NON PATENT LITERATURE DOC	UMENTS		
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) publisher, city and/or country where	date, page(s), volume-iss	* *	T ²
		Bachevalier, J. et al. (2001). Effect	s of selective	neonatal	
		temporal lobe lesions on socioemotio	nal behavior :	in infant	
		rhesus monkeys (<i>Macaca mulatta</i>). Behav 559	. Neurosci. 115	(3), 545-	
		Baron-Cohen, S. et al. (2000). The amy	gdala theory o	f autism.	
		Neurosci. Biobehav. Rev. 24(3), 355-36	4		
		Bast, T. et al. (2001). The ventral	l hippocampus	and fear	
		conditioning in rats. Different anter			
		after tetrodotoxin inactivation and i		e GABA(A)	
		agonist muscimol. Exp. Brain Res. 139(
		Belmont, L.D., and Mitchison, T.J. (19)			
		protein that interacts with tubulin d			
		catastrophe rate of microtubules. Cell Bolshakov, V.Y. et al. (1997). Recru			
		synaptic transmission during the cAMP-			
		LTP at CA3-CA1 synapses in the hippocar 651			
		Bolshakov, V.Y. et al. (2000). Dual MAP opposing forms of long-term plasticit Nat. Neurosci. 3(11),1107-1112			
		Bourtchouladze, R. et al. (1998). Diffe	rent training p	procedures	
		recruit either one or two critical			
		memory consolidation, each of which red	quires protein	synthesis	
		and PKA. Learn. Mem. 5(4), 365-374		7	
		Brauer, A.U. et al. (2001). Perforant regulation of stathmin messenger RNA, RNA, in the adult rat hippocampus. Neur	but not SCG10	messenger	
		Cook, E.H. et al. (1998). Linkage-dis	sequilibrium ma	apping of	
		autistic disorder, with 15q11-13 marks 62(5),1077-1083	ers. Am. J. Hu	m. Genet.	
		Davis, M., and Whalen, PJ. (2001). The	amygdala: vigi	lance and	
		emotion. Mol. Psychiatry 6(1), 13-34			
	_	Dulac, C., and Axel, R. (1995). A			
i		encoding putative pheromone receptors 195-206	in mammals. Ce	11 83(2),	
			(1999). Why		
		plasticity underlying Pavlovian fear co		rs in the	
		basolateral amygdala. Neuron 23(2), 22			
		Frederickson, C.J. et al. (2000). Imp			
		central nervous system: the zinc-conta 130, 1471S-1483S	aining neuron.	J. NUCT.	

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). ²Applicant is to place a checkmark here if English language Translation is attached.

EXAMINER SIGNATURE

Form PT	O-144	9 U.S. Department of Commerce	Application Number	10/582,303
Substitut		Patent and Trademark Office	Filing Date	As §371 national stag of PCT/US04/41388, filed December 9, 200
			First Named Inventor	
INVESTOR	4 A TO 1 C	NI DICCI OCUDE CITATION	Art Unit	Eric Kander et al.
ľ		ON DISCLOSURE CITATION		
(Use severa	al sheets	s if necessary)	Examiner Name	
			Attorney Docket No.	70442-PCT-US
		NON PATENT LITERATURE DOC	UMENTS	
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) publisher, city and/or country where	date, page(s), volume-iss	
		Goddard, A.W. et al. (2001). Reduction	ons in occipita	al cortex
		GABA levels in panic disorder dete	ected with ¹ H	-magnetic
		resonance spectroscopy. Arch. Gen. Psy		
		Hampton, L.L. et al. (1998). Loss of b		
		suppression in gastrin-releasing pep	tide receptor-	deficient
		mice. Proc. Natl. Acad. Sci. USA 95, 3		
		Harrel, A.V. et al. (2001). Transgenic		essing the
		5-HT3 receptor have enhanced learning		
		contextual fear conditioning paradigms	. Soc. Neurosci	. Abstr.,
		Program No. 853.11, 31st Annual Meeting	g, San Diego, C	alifornia
		Hellmich, M.R. (1999). Multiple prote	in kinase patl	nways are
1		involved in gastrin-releasing pept	ide receptor-	regulated
		secretion. J. Biol. Chem. 274(34), 239	01-23909	
		Huang, Y.Y., and Kandel, E.R. (1998).	Postsynaptic	induction
		and PKA-dependent expression of LTP in		
		Neuron 21(1), 169-178		
		Hubank, M., and Schatz, D.G. (1994). Id	entifying diffe	rences in
		mRNA expression by representational		
		cDNA. Nucleic Acids Res. 22(25), 5640-	5648	
		Ishikawa-Brush, Y. et al. (1997). Autis		exostoses
		associated with an X;8 translocation of	ccurring within	the <i>GRPR</i>
		gene and 3' to the SDC2 gene. Hum. Mol	. Genet. 6(8),	1241-1250
		Johansson, B. et al. (2001). Hyper	algesia, anxi	ety, and
		decreased hypoxic neuroprotection in mi	ce lacking the	adenosine
		A1 receptor. Proc. Natl. Acad. Sci. US		
		Kapp, B.S. et al. (1992). Amygda	loid contribu	tions to
		conditioned arousal and sensory informa		
		Amygdala: Neurobiological Aspects of		
ľ		Mental Dysfunction, J.P. Aggleton, ed.	(New York: Wil	ey-Liss),
		pp. 229-254		
		Krezel, W. et al. (2001). Increased		
		plasticity in estrogen receptor β-defi	cient mice. Pr	oc. Natl.
		Acad. Sci. USA 98(21), 12278-12282		
		Kroog, G.S. et al. (1995). Mammalian b	ombesin recept	ors. Med.
		Res. Rev. 15, 389-417		
		LeDoux, J.E. (2000). Emotion circuits in Neurosci. 23, 155-184	in the brain. A	nnu. Rev.
		Lee, K. et al. (1999). Bombesin-like	pentides depola	arize rat
		hippocampal interneurones through interbombesin receptors. J. Physiol. 518(3)	eraction with s	
EXAMINE	R			

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). Applicant is to place a checkmark here if English language Translation is attached.

Page 4 of 6

Form PT	O-144	9 U.S. Do	epartment of Commerce	Application Number	10/582,303	
Substitut			and Trademark Office	Filing Date	As §371 nation	
					of PCT/US04/	
					filed Decembe	
				First Named Inventor	Eric Kandel e	t al.
INFORM	1ATIC	ON DISCLOSURE	CITATION	Art Unit		
(Use severa	(Use several sheets if necessary) Examiner Name					
	Attorney Docket No. 70442-PCT-US					
ļ		NON	PATENT LITERATURE DOC	CUMENTS		
Examiner Initials	Cite No. ¹	Include name of the autitem (book, magazine,	thor (in CAPITAL LETTERS), title of th journal, serial, symposium, catalog, etc.) publisher, city and/or country where	date, page(s), volume-iss	ate), title of the ue number(s),	T ²
		Low, K. et al. selective atte	(2000). Molecular and ne nuation of anxiety. Scie	euronal substrat	e for the 4	
	-	Mahanty, N.K.	, and Sah, P. (1998).	Calcium-permea	able AMPA	
		receptors media	ate long-term potentiations 394, 683-687			
		Malleret, G.	et al. (1999). 5-HT1B			
		exhibit increamemory perform 19(14), 6157-6		ter maze. J.	d spatial Neurosci.	
		McKernan, M.G conditioning			7). Fear synaptic	
		currents in vi	tro. Nature 390, 607-611	L		
		properties of	. et al. (2000). Sedat benzodiazepines are m (1) subtype. Nat. Neuros	ediated by the	e GABA(A)	
		the release of	al. (1998). Aversive and corticotropin-releasin at the central nucleu 4758-4766	g hormone and	bombesin-	
		Mermelstein, Presponse elementalcium channe	G., et al. (2000). Critent-binding protein phoels supports a selectivaction potentials. J. Ne	esphorylation of the control of the	on L-type EPSPs in	
		Parent, M.B	. et al. (2002).	Effects	of the	
		metabolite phe aminobutyric a 63, 57-64	/antipanic drug phenel enylethylidenehydrazine cid levels in the striat	on extracellul tum. Biochem. F	ar gamma- harmacol.	
		circuitries in functions of t	et al. (1997). Organizat the rat: an emerging fra he amygdala. Trends Neur	amework for underosci. 20(11),	erstanding 517-523	
		animal model	al. (1998). Serotonin r of anxiety-related dison), 14476-14481	rder. Proc. Na	tl. Acad.	-
		basolateral am negative cAMP forebrain. Eur	nygdala in transgenic mi response element-bind . J. Neurosci. 12, 2534-	ing protein (-2546	dominant- (CREB) in	
		Rogan, M.T. associative log	et al. (1997). Fear ng-term potentiation in t			
EXAMINE SIGNATU			13			

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). Applicant is to place a checkmark here if English language Translation is attached.

Form PTO-1449 U.S. D		19 U.S. Department of Commerce	Application Number	10/582,303	
Substitute Pat		Patent and Trademark Office	Filing Date	As §371 nation	nal stage
				of PCT/US04/4	
				filed December	
			First Named Inventor	Eric Kandel et	t al.
		ON DISCLOSURE CITATION	Art Unit		
(Use severa	d sheet	s if necessary)	Examiner Name		
			Attorney Docket No.	70442-PCT-US	3
		NON PATENT LITERATURE DOC	UMENTS		
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) publisher, city and/or country where	date, page(s), volume-issue published.	ue number(s),	T ²
		Romanski, L.M., and LeDoux, J.E. (199			
		thalamo-amygdala and thalamo-cortico			
		auditory fear conditioning. J. Neurosc			
		Schaeren-Wiemers, N., and Gerfin-Mose protocol to detect transcripts of various			
		levels in neural tissue and cult		in situ	
		hybridization using digoxigenin-la Histochemistry 100, 431-440		probes.	
1		Sharif, T.R. et al. (1997). Functional	expression of	bombesin	
		receptor in most adult and pediatric			
•		lines; role in mitogenesis and in st			
		activated protein kinase pathway. Mol. 119-130	Cell. Endocri	no1. 130,	
		Steele, P.M., and Mauk, M.D. (1999). In	nhibitory contr	ol of IMP	
}		and LTD: stability of synapse strengt			
ļ		1559-1566	ii. o. nearophy.	101. 01/	
		Trepel, C., and Racine, R.J. (2000). neocortical long-term potentiation in Synapse 35(2), 120-128			
		Tsvetkov, E. et al. (2002). Fear cond	ditioning occlu	ides LTP-	
		induced presynaptic enhancement of syna			
4		cortical pathway to the lateral amygdal			
		Wada, E. et al. (1997). Generation and lacking gastrin-releasing peptide rece Res. Commun. 239, 28-33	eptor. Biochem.		
		Wang, C. et al. (2001). Role of NMI		and GABA	
		receptors in signal propagation in the Neurophysiol. 86, 1422-1429			
		Weisskopf, M.G., and LeDoux, J.E. (1999) of NMDA receptors at subcortical as			
		principal cells of the lateral amygdal			
		930-934	a. o. Neurophy.	3101. 01/	
		Weisskopf, M.G. et al. (1999). L-type	e voltage-gated	d calcium	
		channels mediate NMDA-independent	associative	long-term	
		potentiation at thalamic input synaps	es to the amyo	ıdala. J.	
		Neurosci. 19(23), 10512-10519			
		Woodson, W. et al. (2000). Afferents fr			
		synapse on inhibitory interneurons in the amygdala. Synapse 38(2), 124-137	the lateral nu	icleus of	
		Yu, B., and Shinnick-Gallagher, P. (199	7) Dihydropyri	dine- and	
		neurotoxin-sensitive and -insensitive	e calcium cur	rents in	
		acutely dissociated neurons of the ra			
		Neurophysiol. 77(2), 690-701			U U
EXAMINEI SIGNATUR		DATE CONSIDERED			

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 'Applicant's unique citation designation number (optional). ²Applicant is to place a checkmark here if English language Translation is attached.

Page 6 of 6

Form PT	O-144	9 U.S. D	epartment of Comn	nerce	Application Number	r 10/582,303	
Substitut	te	Patent	and Trademark Of	ffice	Filing Date	As §371 nation of PCT/US04	/41388,
					First Named Inver	filed Decemb	
INFORM	AATIC	N DISCLOSURE	CITATION		Art Unit	HOI ETIC Kanuer	et ai.
		s if necessary)	CHARION		Examiner Name		
(Use sever	al succe	il liecessai y j			Attorney Docket	No. 70442-PCT-U	21
		NON	PATENT LITERA			10. 1.0442 202 0) 55
Examiner Initials*	Cite No. ¹	Include name of the au	athor (in CAPITAL LETT , journal, serial, symposiu publisher, city and/o	ERS), title of the	e article (when approdate, page(s), volume		T ²
		issued by t International	Preliminary Rep he Internation	port on Pa hal Burea thority o	tentability u on beha on June 12	lf of the , 2006 in	1
	; L						
EXAMINE: SIGNATUR			DATE CONSIDERED				

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional). Applicant is to place a checkmark here if English language Translation is attached.